

(FILE 'HOME' ENTERED AT 13:27:00 ON 12 DEC 2002)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 13:27:38 ON 12 DEC 2002

L1 257832 S CYSTEINE OR CYSTINE  
L2 23744 S L1 AND OXIDAT?  
L3 874904 S L2 AND STABILIZ? OR STABILIT?  
L4 1366 S L2 AND DEGRAD?  
L5 151 S L4 AND ANTIOXIDANT#  
L6 1 S L5 AND INSULIN  
L7 97 S L5 AND PY=<1999  
L8 64 DUP REM L7 (33 DUPLICATES REMOVED)  
L9 1339260 S STABILIZ? OR STABILIT#  
L10 57657 S L9 AND CYSTEINE OR CYSTINE  
L11 5641 S L10 AND OXIDAT?  
L12 155 S L11 AND INSULIN  
L13 129 S L12 AND PY=<1999  
L14 94 DUP REM L13 (35 DUPLICATES REMOVED)  
L15 827 S L10 AND REDUCING AGENT#  
L16 19 S L15 AND INSULIN  
L17 13 DUP REM L16 (6 DUPLICATES REMOVED)  
L18 32003 S L15 AND STORAGE OR STORING  
L19 51 S L15 AND STABILIZATION  
L20 33 DUP REM L19 (18 DUPLICATES REMOVED)

3 CAPLUS COPYRIGHT 2002 ACS

AN 1995:446844 CAPLUS

DN 122:182020

TI **Stabilization** of human islet glutamic acid decarboxylase65 with  
**reducing agents**, detergents, alcohols, and/or divalent  
metal ions

IN Hejnaes, Kim; Moody, Alister J.; Marshall, Michael Owen

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9504137	A1	19950209	WO 1994-DK289	19940719
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP,				
	KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI,				
	SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,				
	NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD,				
TG	AU 9472268	A1	19950228	AU 1994-72268	19940719
	EP 717776	A1	19960626	EP 1994-921606	19940719
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
PRAI	DK 1993-880		19930728		
	WO 1				

L20 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2002 ACS

AN 1996:599137 CAPLUS

DN 125:215705

TI **Stabilized** transglutaminases, method of preparing them, and  
their use in pharmaceuticals

IN Metzner, Hubert; Karges, Hermann

PA Behringwerke AG, Germany

SO Ger. Offen., 11 pp. ...

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	DE 19508192	A1	19960912	DE 1995-19508192	19950309
	EP 733702	A1	19960925	EP 1996-101959	19960210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	NO 9600813	A	19960910	NO 1996-813	19960228
	AU 9647915	A1	19960919	AU 1996-47915	19960306
	CA 2171266	AA	19960910	CA 1996-2171266	19960307
	JP 08245418	A2	19960924	JP 1996-51439	19960308
	CN 1137564	A	19961211	CN 1996-102737	19960308
	US 6204036	B1	20010320	US 1997-999702	19971222
	AU 738891	B2	20010927	AU 2000-35419	20000519
PRAI	DE 1995-19508192	A	19950309		

L20 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2002 ACS  
AN 1954:48776 CAPLUS  
DN 48:48776  
OREF 48:8628i,8629a-g  
TI Mercaptans and disulfides-some physics, chemistry, and speculation  
AU Calvin, Melvin  
CS Univ. of California, Berkeley  
SO U.S. Atomic Energy Comm. UCRL-2438 (1954) 3-39  
DT Journal  
LA

L20 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2002 ACS

AN 1999:448905 CAPLUS

DN 131:127189

TI **Stabilization** of enzymes in blood samples using **reducing agents**

IN Yoshino, Manabu; Kamiyama, Michinobu

PA Eiken Chemical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 11192084	A2	19990721	JP 1997-367617	19971229

L20 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2002 ACS

AN 1998:105917 CAPLUS

DN 128:151119

TI **Stabilization** of bilirubin oxidase with **reducing agents**

IN Sato, Kazuhiko

PA Eiken Chemical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 10 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 10042869	A2	19980217	JP 1996-220295	19960801

L17 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2002 ACS  
AN 1930:19732 CAPLUS  
DN 24:19732  
OREF 24:2135e-h  
TI The chemistry of **insulin**  
AU Freudenberg, V. Karl; Dirscherl, Wilhelm; Eyer, Hermann  
SO Z. physiol. Chem. (1930), 187, 89-119  
DT Journal  
LA

L20 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2002 ACS

AN 1997:400033 CAPLUS

DN 127:31253

TI **Stabilization** of IgM-containing reagent solution with  
**reducing agents** and sulfhydryl-modifying agents for  
immunoassay of IgM-type antibodies

IN Yoshimura, Toru

PA Dainabot Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	JP 09127112	A2	19970516	JP 1995-303302	19951030



L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2002 ACS  
 AN 2001:330570 CAPLUS  
 DN 135:272164  
 TI Effects of two physiological redox systems on wheat proteins  
 AU Jarraud, F.; Kobrehel, K.  
 CS Unite Biochim. Biol. Mol. Cereales, I.N.R.A., Montpellier, 34 060, Fr.  
 SO Spec. Publ. - R. Soc. Chem. (2000), 261(Wheat Gluten), 262-266  
 CODEN: SROCD0; ISSN: 0260-6291  
 PB Royal Society of Chemistry  
 DT Journal  
 LA English  
 CC 17-11 (Food and Feed Chemistry)  
 AB The two endogenous enzyme systems in wheat, which can modify the redox state of proteins, are NADP-dependent thioredoxin system and the glutathione system (NGS). The specific action of these two systems on wheat gluten protein fractions were described and their effects were compared to the effects of two chem. **reducing agents**, such as 2-mercaptoethanol and dithiothreitol (DTT). The stronger effect of NTS on HMW glutenins, and in general on **storage** proteins, compared to DTT, was esp. important in relation to the potential involvement of thioredoxin in wheat processing. Dithiol reducing systems showed much stronger effect on wheat proteins than monothiols, indicating that disulfide bonds of most wheat proteins were dithiol specific. Thioredoxin, the **reducing agent** of the endogenous NTS system, was the most efficient in S-S bonds redn. of wheat proteins, particularly gliadins, low and high mol. wt. glutenins. The reoxidized reduced proteins tended to form large aggregates, for which the presence of free-SH groups seemed to be important. The reducing conditions and the degree of redn. of the proteins with the different **reducing agents** had effects, but relatively small ones, on the electrophoretic patterns of the proteins, indicating relatively small conformational modifications.  
 ST wheat protein redox system  
 IT Disulfide group  
 Wheat  
 (physiol. redox systems effect on wheat proteins)  
 IT Thioredoxins  
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)  
 (physiol. redox systems effect on wheat proteins)  
 IT **Albumins**, biological studies  
 RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
 (physiol. redox systems effect on wheat proteins)  
 IT Gliadins  
 RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
 (physiol. redox systems effect on wheat proteins)  
 IT Globulins, biological studies  
 RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
 (physiol. redox systems effect on wheat proteins)  
 IT Glutenins  
 RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
 (physiol. redox systems effect on wheat proteins)  
 IT Proteins, general, biological studies

RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
 (physiol. redox systems effect on wheat proteins)

IT 70-18-8, Glutathione, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BOC  
 (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)  
 (physiol. redox systems effect on wheat proteins)

IT 60-24-2, 2-Mercaptoethanol 3483-12-3, Dithiothreitol  
 RL: BAC (Biological activity or effector, except adverse); FFD (Food or feed use); BIOL (Biological study); USES (Uses)  
 (physiol. redox systems effect on wheat proteins)

RE.CNT 6  
 RE  
 (1) Anon; Handbook of breadmaking technology 1990, P848  
 (2) Gobin, P; Thesis 1995, P121  
 (3) Hamauzu, Z; Cereal Chem 1979, V56, P513 CAPLUS  
 (4) Kobrehel, K; Cereal Chem 1977, V54, P833 CAPLUS  
 (5) Kobrehel, K; Plant Physiol 1992, V99, P919 CAPLUS  
 (6) Mifflin, B; Seed Proteins 1983, P255 CAPLUS

L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2002 ACS  
 AN 1996:625641 CAPLUS  
 DN 125:269843  
 TI Stabilizing solutions for proteins and peptides  
 IN Flaa, Cathy; Sabucedo, Alberto; Chin, Bruce; Bauer, Roger  
 PA Dade International Inc., USA  
 SO PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C12N009-96  
 ICS G01N033-68; G01N033-531  
 CC 9-2 (Biochemical Methods)  
 Section cross-reference(s): 7

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9627661	A1	19960912	WO 1996-US3034	19960306
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6165981	A	20001226	US 1995-400158	19950307
	CA 2189737	AA	19960912	CA 1996-2189737	19960306
	AU 9650929	A1	19960923	AU 1996-50929	19960306
	AU 698790	B2	19981105		
	EP 759074	A1	19970226	EP 1996-907187	19960306
	EP 759074	B1	19980708		
	R: DE, ES, FR, IT				
	JP 10500704	T2	19980120	JP 1996-527023	19960306
	ES 2121479	T3	19981116	ES 1996-907187	19960306
PRAI	US 1995-400158	A	19950307		
	WO 1996-US3034	W	19960306		
AB	Disclosed are compns. for stabilizing proteins and fragments of the proteins. The compn. contains buffer, salt, <b>reducing agents</b> , chelating agents and stabilizing proteins. The compn. may be used to prep. highly stable diagnostic calibrators or controls and is particularly useful for calibrators or controls for cardiac markers such as troponin. Since the matrix contg. the calibrator is not human serum-derived, the user and manufg. personnel are not exposed to blood products which may spread disease. The matrix also stabilizes the analyte in liq. form for extended periods of time. The formulations can be lyophilized or frozen and then reliably reconstituted or thawed for up to at least 9 mo shelf <b>storage</b> with very little variation in calibration. After reconstitution or thawing, the analyte is stable for				

up to 3 wk at 2-8.degree..

ST protein stabilization cardiac marker; troponin stabilization  
**albumin** gelatin EDTA trehalose

IT Gelatins, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (blocking agent; stabilizing solns. for proteins and peptides)

IT **Albumins**, uses  
 Caseins, uses  
 Ovalbumins  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (stabilizer; stabilizing solns. for proteins and peptides)

IT Buffer substances and systems  
 Chelating agents  
**Reducing agents**  
 (stabilizing solns. for proteins and peptides)

IT Salts, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (stabilizing solns. for proteins and peptides)

IT Proteins, processes  
 RL: PEP (Physical, engineering or chemical process); PROC (Process)  
 (stabilizing solns. for proteins and peptides)

IT Troponins  
 RL: PEP (Physical, engineering or chemical process); PROC (Process)  
 (stabilizing solns. for proteins and peptides)

IT Troponins  
 RL: PEP (Physical, engineering or chemical process); PROC (Process)  
 (I, stabilizing solns. for proteins and peptides)

IT 50-99-7, Glucose, uses 57-50-1, Sucrose, uses 59-23-4, Galactose,  
 uses  
 63-42-3, Lactose 69-79-4, Maltose 99-20-7, Trehalose 499-40-1,  
 Isomaltose 528-50-7, Cellobiose 585-99-9, Melibiose 1109-28-0,  
 Maltotriose 3458-28-4, Mannose 13133-07-8, Nystose 14417-51-7,  
 Mannobiose 34612-38-9, Maltotetraose 34620-76-3, Maltopentaose  
 34620-77-4, Maltohexaose 34620-78-5, Maltoheptaose  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (bulking agent; stabilizing solns. for proteins and peptides)

IT 60-00-4, EDTA, uses 67-42-5, EGTA 77-92-9, uses 144-62-7,  
 Ethanedioic acid, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (chelating agent; stabilizing solns. for proteins and peptides)

IT 60-23-1, 2-Aminoethanethiol 60-24-2, 2-Mercaptoethanol 616-91-1,  
 N-Acetylcysteine 3483-12-3, Dithiothreitol  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (**reducing agent**; stabilizing solns. for proteins  
 and peptides)

IT 182300-79-4 182326-18-7  
 RL: PEP (Physical, engineering or chemical process); PROC (Process)  
 (stabilizing solns. for proteins and peptides)

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2002 ACS  
 AN 1992:403854 CAPLUS  
 DN 117:3854  
 TI Stabilized anoxic diagnostic reagent solution  
 IN Saldivar, Louis, Jr.; England, Barbara J.  
 PA Abbott Laboratories, USA  
 SO PCT Int. Appl., 17 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM C12Q001-54  
 ICS G01N033-00; A61K037-00  
 CC 9-15 (Biochemical Methods)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9207088	A1	19920430	WO 1991-US7629	19911018

W: AU, CA, JP, KR  
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE  
AU 9188745 A1 19920520 AU 1991-88745 19911018  
EP 541729 A1 19930519 EP 1991-919544 19911018  
EP 541729 B1 19961227  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE  
AT 146821 E 19970115 AT 1991-919544 19911018  
ES 2098377 T3 19970501 ES 1991-919544 19911018  
US 5401639 A 19950328 US 1992-935677 19920825  
PRAI US 1990-600797 19901022  
WO 1991-US7629 19911018  
AB A stabilized anoxic diagnostic reagent soln. comprises an O labile reagent  
(e.g. hormones, lipids, steroids, **reducing agents**, etc.), glucose oxidase, glucose, a H donor, sterile membrane fragments derived from bacteria having membranes contg. an O transfer system, and a reagent binding agent (e.g. **albumin**). The stabilized reagent has .gtoreq.6 mo **storage** stability at 2-8.degree. and an open vial stability of .gtoreq.3 wk. A reagent soln. contg. bilirubin as the oxygen labile reagent also included EtOH, Brij 35, bistrispropane, glucose, BHT, D-lactate, bovine serum **albumin**, gentamicin, Oxyrase (membrane system), and glucose oxidase.  
ST anoxic diagnostic reagent soln; bilirubin stable anoxic std soln  
IT Pharmaceuticals  
**Reducing agents**  
Antibodies  
Antigens  
Flavanols  
Hormones  
Lipids, uses  
Steroids, uses  
RL: ANST (Analytical study)  
(as oxygen labile reagent, stabilized anoxic diagnostic reagent soln. contg.)  
IT Membrane, biological  
(fragments of, contg. oxygen transfer system for oxygen redn., stabilized anoxic diagnostic reagent soln. contg.)  
IT Radicals, miscellaneous  
RL: MSC (Miscellaneous)  
(scavengers of, stabilized anoxic diagnostic reagent soln. contg.)  
IT Antioxidants  
Alcohols, uses  
RL: USES (Uses)  
(stabilized anoxic diagnostic reagent soln. contg.)  
IT Standard solutions, analytical  
(stabilized anoxic diagnostic reagent soln. contg. oxygen-labile reagent for)  
IT **Albumins**, uses  
RL: USES (Uses)  
(stabilized anoxic diagnostic reagent soln. contg., as reagent binding agent)  
IT Analysis  
(stabilized anoxic diagnostic reagent soln. for)  
IT 635-65-4, Bilirubin, uses  
RL: USES (Uses)  
(as oxygen labile reagent, stabilized anoxic diagnostic reagent soln. contg.)  
IT 1333-74-0, Hydrogen, uses  
RL: USES (Uses)  
(donor, stabilized anoxic diagnostic reagent soln. contg.)  
IT 7732-18-5, Water, reactions  
RL: RCT (Reactant)  
(membrane fragments contg. oxygen transfer system for oxygen redn. to, stabilized anoxic diagnostic reagent soln. contg.)  
IT 7782-44-7, Oxygen, uses  
RL: USES (Uses)

(reagent labile to, stabilized anoxic diagnostic reagent soln. contg.)  
 IT 9001-05-2, Catalase 9001-37-0, Glucose oxidase 9002-92-0, Brij 35  
 9035-73-8, Oxidase 10326-41-7, uses 64431-96-5, Bistrispropane  
 140608-85-1, Oxyrase 50-99-7, Glucose, uses 64-17-5, Ethanol, uses  
 128-37-0, BHT, uses  
 RL: ANST (Analytical study)  
 (stabilized anoxic diagnostic reagent soln. contg.)

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS  
 AN 1986:39703 CAPLUS  
 DN 104:39703  
 TI Stable composition of interleukin-2  
 IN Mikura, Yasushi; Asada, Kensuke; Toguchi, Hajime  
 PA Takeda Chemical Industries, Ltd. , Japan  
 SO Eur. Pat. Appl., 27 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 IC ICM A61K037-02  
 CC 63-3 (Pharmaceuticals)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 158487	A2	19851016	EP 1985-302176	19850328
	EP 158487	A3	19870819		
	EP 158487	B1	19910828		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 60215631	A2	19851029	JP 1984-71568	19840409
	JP 03061652	B4	19910920		
	JP 60222424	A2	19851107	JP 1985-13226	19850125
	JP 03078847	B4	19911217		
	JP 61197527	A2	19860901	JP 1985-37184	19850225
	ZA 8502302	A	19861126	ZA 1985-2302	19850327
	AT 66612	E	19910915	AT 1985-302176	19850328
	CN 85101301	A	19860723	CN 1985-101301	19850401
	CN 1019453	B	19921216		
	DK 8501488	A	19851010	DK 1985-1488	19850402
	AU 8540839	A1	19851017	AU 1985-40839	19850404
	AU 579359	B2	19881124		
	IL 74823	A1	19890731	IL 1985-74823	19850404
	CA 1285478	A1	19910702	CA 1985-478351	19850404
	ES 542028	A1	19851216	ES 1985-542028	19850408
	US 4645830	A	19870224	US 1985-720754	19850408
	US 4812557	A	19890314	US 1986-931704	19861117
PRAI	JP 1984-71568		19840409		
	JP 1985-13226		19850125		
	JP 1985-37184		19850225		
	EP 1985-302176		19850328		
	US 1985-720754		19850408		

AB Interleukin-2 is stabilized by treatment with human serum **albumin** (HSA) and/or a reducing compd., prior to freezing or lyophilization. The pH of the compn. must be 3-6. Thus, 0.5 mL interleukin-2 (7680 units)

was treated with 5.0 mL HSA and 2 mg glutathione, after sterile filtration. The compn. (pH 4.1) was placed in a vial, frozen at -40.degree., lyophilized, and the vial filled with N2. After 1 mo **storage**, the soln. was clear, and interleukin-2 maintained 85% of its potency.

The compn. should be preferably salt free.

ST interleukin 2 stabilization; **albumin** interleukin 2 stabilization

IT **Reducing agents**

(interleukin-2 stabilization by **albumin** and)

IT **Albumins**, blood serum

RL: BIOL (Biological study)

(interleukin-2 stabilization by **reducing agents** and)

IT Lymphokines and Cytokines  
 RL: PROC (Process)  
 (interleukin 2, stabilization of, with human serum **albumin**  
 and **reducing agents**)

IT 50-81-7, biological studies 62-46-4 70-18-8, biological studies  
 616-91-1  
 RL: BIOL (Biological study)  
 (interleukin-2 stabilization by **albumin** and)

L6 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS

AN 1983:427998 CAPLUS

DN 99:27998

TI **Storage**-stable, crosslinked hemoglobin preparation with high  
 oxygen transport capacity

IN Bonhard, Klaus; Kothe, Norbert

PA Biotest-Serum-Institut G.m.b.H., Fed. Rep. Ger.

SO Ger. Offen., 25 pp.

CODEN: GWXXBX

DT Patent

LA German

IC A61K037-14; A61K031-40

CC 63-3 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3144705	A1	19830519	DE 1981-3144705	19811111
	DE 3144705	C2	19831208		
	EP 78961	A2	19830518	EP 1982-109808	19821023
	EP 78961	A3	19830727		
	EP 78961	B1	19861015		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 22803	E	19861115	AT 1982-109808	19821023
	JP 58135818	A2	19830812	JP 1982-193572	19821105
	JP 03065326	B4	19911011		
	US 4777244	A	19881011	US 1987-47819	19870508
PRAI	DE 1981-3144705		19811111		
	EP 1982-109808		19821023		
	US 1982-439473		19821105		

AB A blood substitute is prepd. by treating a stroma-free Hb soln. with an  
 O-consuming **reducing agent** (neutralized ascorbic acid)  
 to reduce the pO<sub>2</sub> to 0 mbar, mixing with a biol. effector (pyridoxal  
 phosphite or inositol hexaphosphate), and crosslinking with a C3-8  
 dialdehyde at pH 6-8. The product was reduced with a carbonyl-specific  
 reagent (NaBH<sub>4</sub>), dild. with H<sub>2</sub>O, treated with activated C, and  
 ultrafiltered. The product can be stabilized with a **reducing**  
**agent**. Thus, an ultrafiltered Hb soln. contg. 19.6% Hb was added  
 to a 4-fold molar excess of neutralized ascorbic acid, sterilized by  
 filtration, and allowed to stand 24 h. The soln., 842 mL, was cooled,  
 mixed with NaH<sub>2</sub>PO<sub>4</sub>-Na<sub>2</sub>HPO<sub>4</sub> and 2.2 g pyridoxal phosphate for 1 h, and

then

13.9 mL 10% glutaraldehyde was stirred in for 1 h, followed by 1.34 g  
 NaBH<sub>4</sub>. The foaming soln. was dild. with 6 L H<sub>2</sub>O after 30 min, treated  
 with 10 g activated C/L for 1 h, and filtered. The soln. was concd. by  
 ultrafiltration to 10-11%, and mixed with 115 mL 20 human **albumin**  
 to adjust osmotic pressure, and then with NaCl 3.32, glucose 14.5, NaHCO<sub>3</sub>  
 1.66, KCl 0.26, MgSO<sub>4</sub> 0.16, and neutralized ascorbic acid 0.61 g before  
 sterilization by filtration. The product was 660 mL of a soln. contg.  
 8.5% Hb and 5.1% relative met-Hb.

ST Hb blood substitute; inositol phosphate Hb; pyridoxal phosphate Hb

IT Blood substitutes and Plasma expanders

(Hb reaction products with inositol hexaphosphate or pyridoxal  
 phosphate prepn. and formulation for)

IT Hemoglobins

RL: PREP (Preparation)

(reaction products with inositol hexaphosphate or pyridoxal phosphate,  
 crosslinked reduced, prepn. and formulation of, for blood substitutes)

IT 54-47-7DP, reaction products with Hb 83-86-3DP, reaction products with  
Hb  
RL: PREP (Preparation)  
(crosslinked, prepn. and formulation of, for blood substitutes)